

# LDRD Project : Measurement of Molecular Shape Using X-ray Scattering

## Objectives

- establish an x-ray scattering facility at the ALS for measurement of molecular shape
  - maintain and enhance our position as a leading center in structural biology
  - bring a broader program in nanoscience to the lab: create strong links to the Molecular Foundry

## Plan

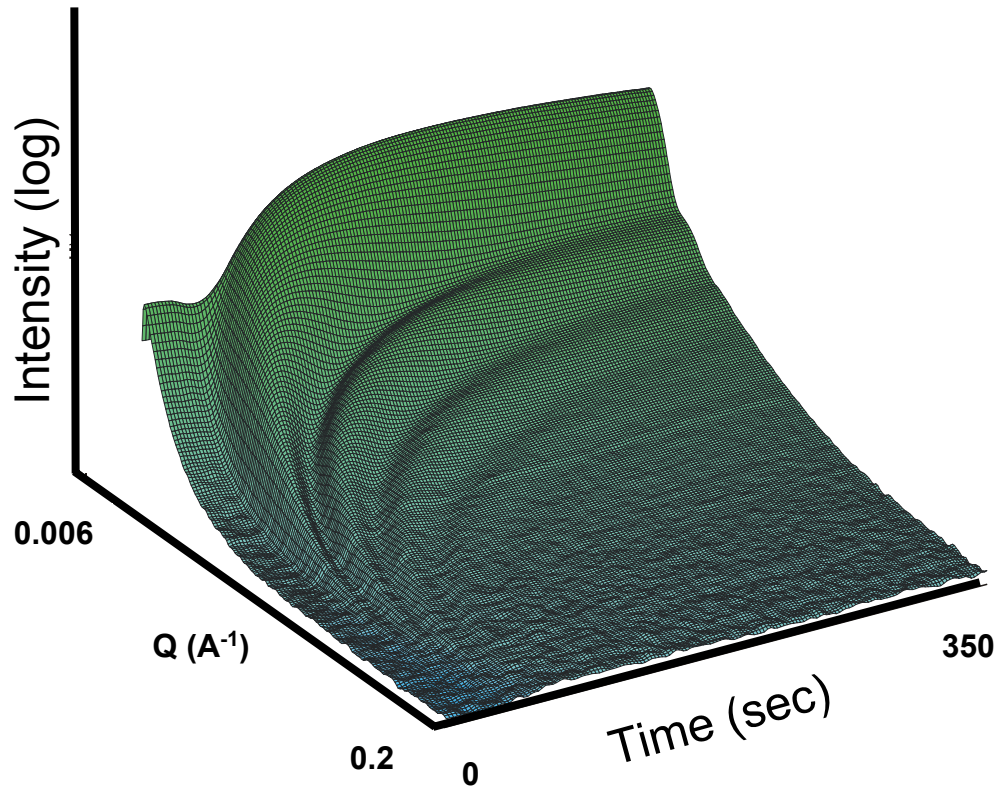
- re-use an existing beamline at ALS + detectors from BCSB/PBD: a \$2M investment
  - build vigorous self sustaining bio and nanoscience programs over the 2 years of this LDRD

## PIs and collaborators (ALS, PBD, MSD, Caltech, UCB, UCSB)

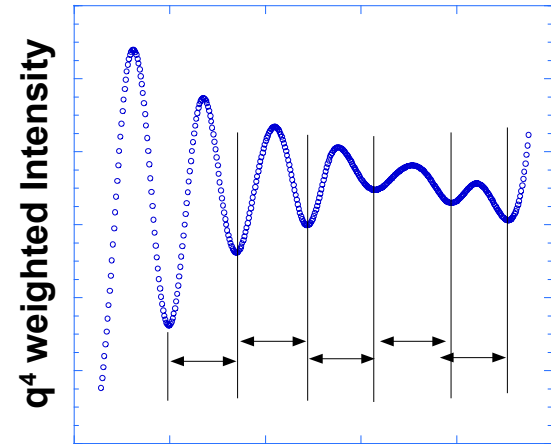
- H. A. Padmore (ALS), M. Marcus (ALS), W. Bras (ESRF),
- J. Kuriyan (UCB), J. Berger (UCB), E. Nogales (UCB), T. Alber (UCB). P. Adams (BCSB / PBD)
- J. Kornfield (Caltech), E. Kramer (UCSB), N. Balsara (UCB / MSD), R. Segalman (UCB / MSD)

# Dynamics of Nucleation : Corderite Glass

(G. N. Greaves, W. Bras, et al  
*Faraday Discuss.*, 2002, **122**, 299–314)

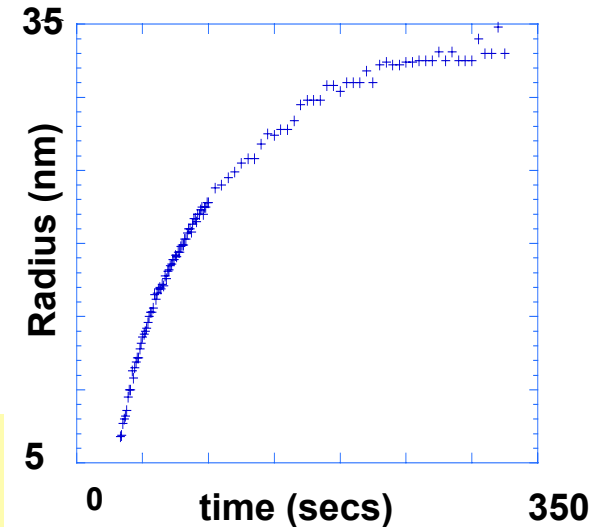


Oscillation period gives domain size



Scattering angle

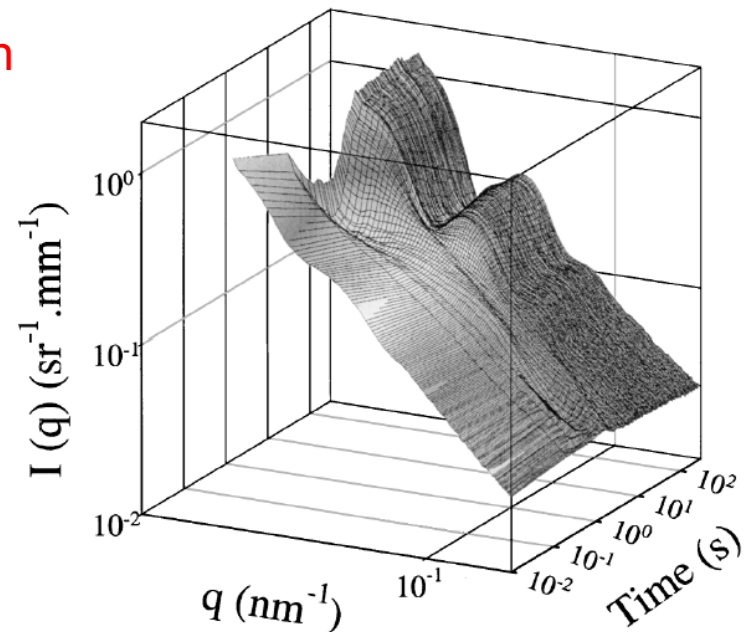
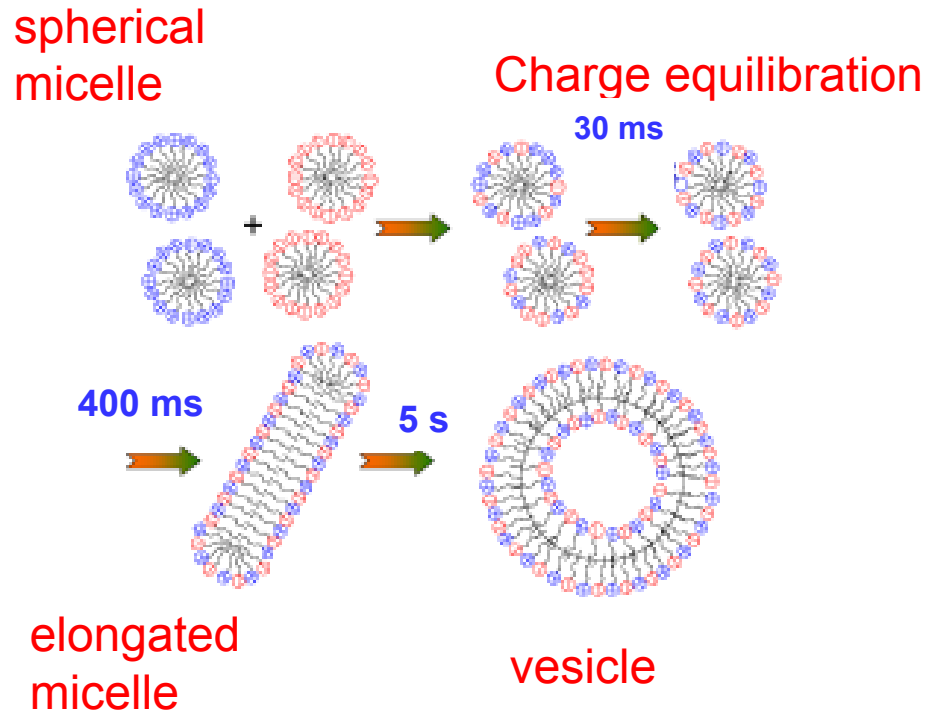
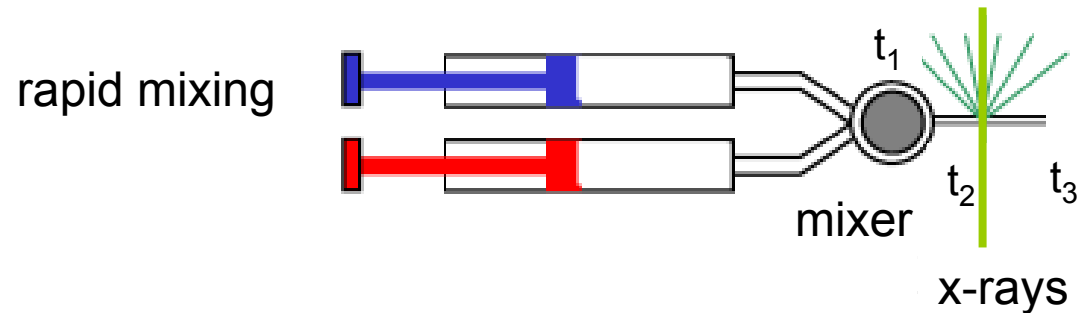
Dynamics of growth can be measured



- glass nucleates into small crystalline domains
- domain growth dynamics can be studied at temperature

# Dynamics of Molecular Assembly

What structural intermediates are formed in the assembly of vesicles?



Schmoelzer et al, PRL 88,258301 (2002)

# Structure of Large Protein Complexes: DnaG

DnaG: Bacterial Primase

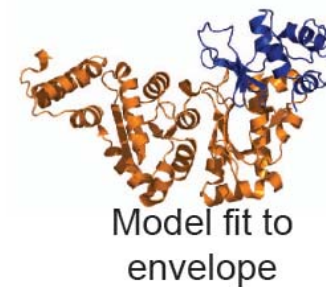
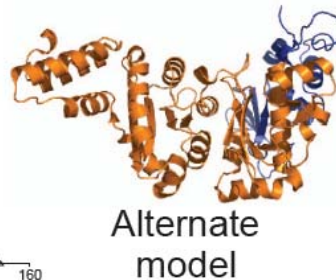
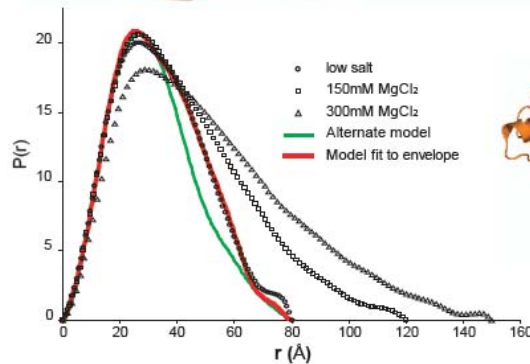
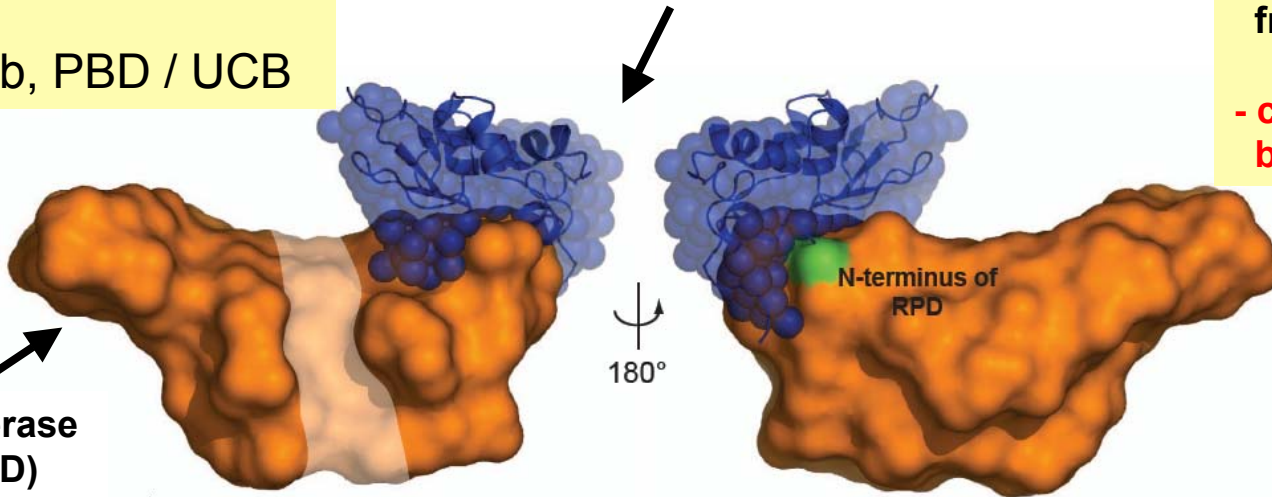
Berger Lab, PBD / UCB

Zinc Binding Domain (ZBD)

- RPD and ZBD atomic structures known from crystallography

- complex could not be crystalized

RNA Polymerase Domain (RPD)



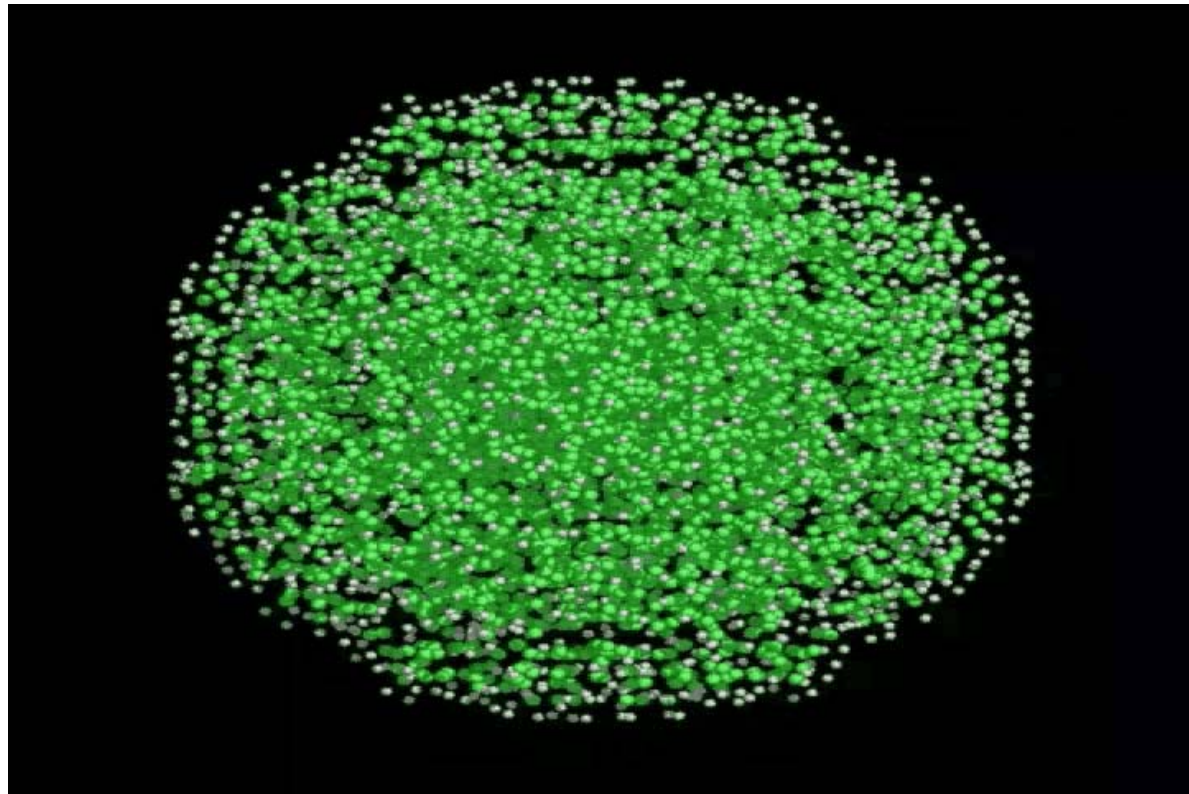
- SAXS allows the relative RPD-ZBD positions to be determined

- how close are the RPD-ZBD contacts

- how do the contacts change when changing physiological conditions

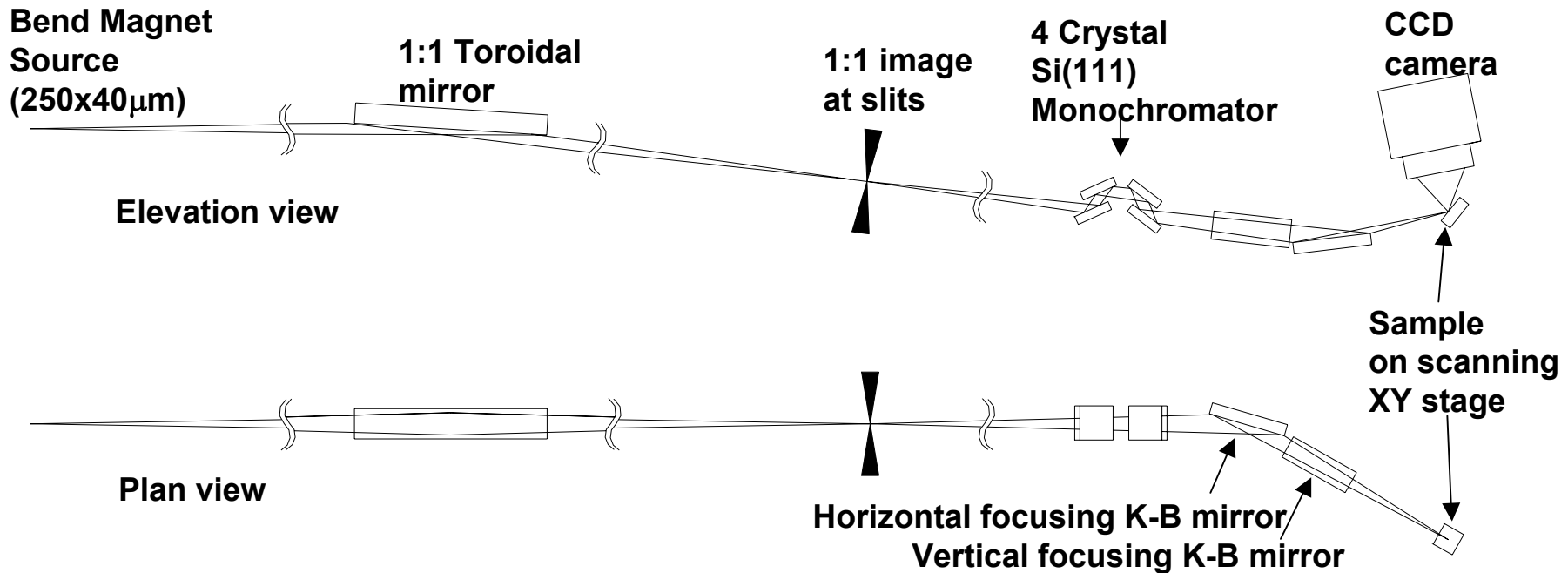
# CaMKII $\alpha$ Holoenzyme: Reconstruction from SAXS Data

Kuriyan Lab, PBD / UCB



- CaMKII $\alpha$  holoenzyme: kinase involved in cell signaling related to synaptic pathways
  - mutations in this protein affect memory
- SAXS allows molecular envelope to be found (known symmetry imposed)
  - has proven impossible to crystallize, or address with single particle EM

# Schematic layout of Beamline 7.3.3 at the ALS

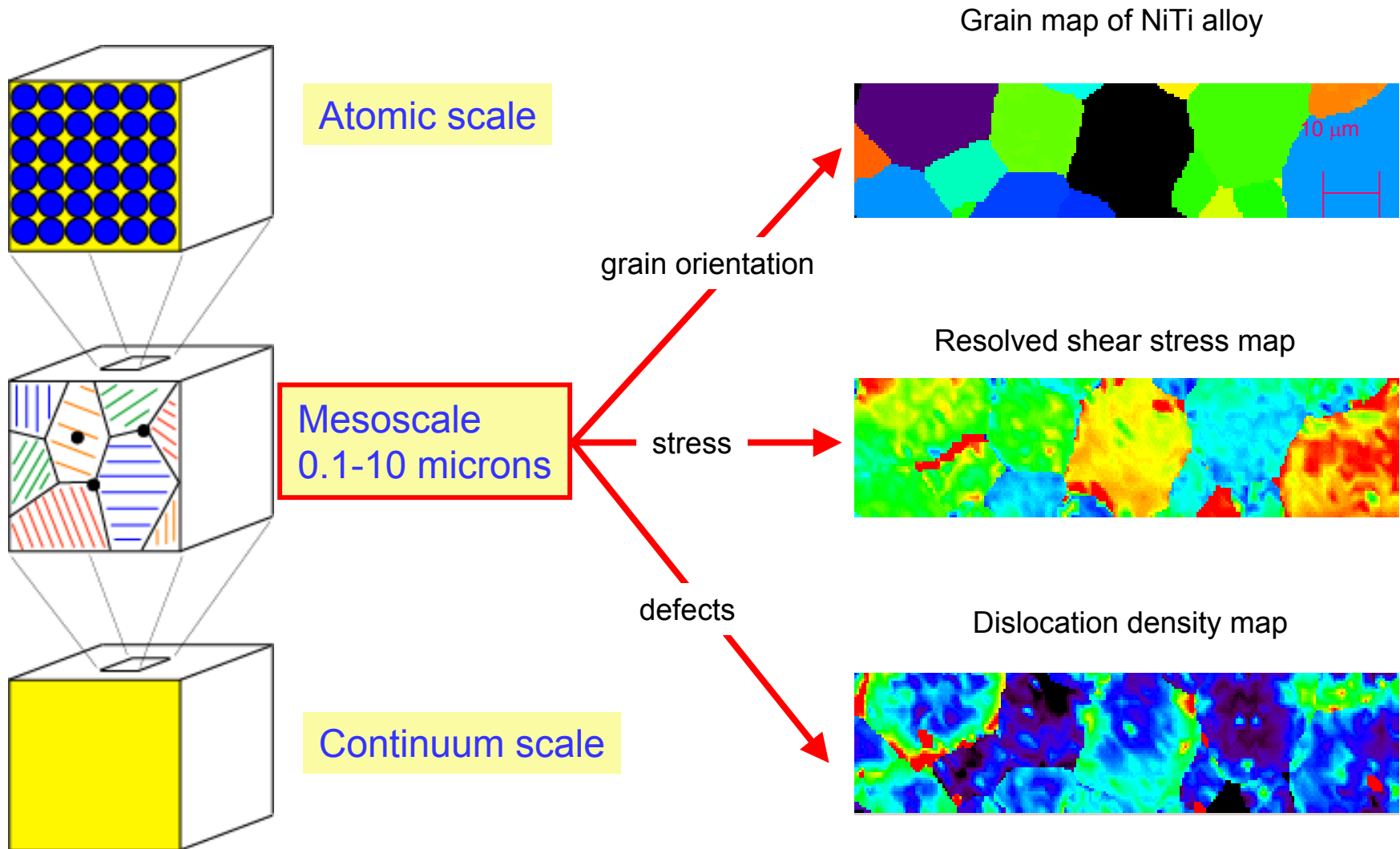


Beam size on sample:  $0.8 \times 0.8 \mu\text{m}^2$

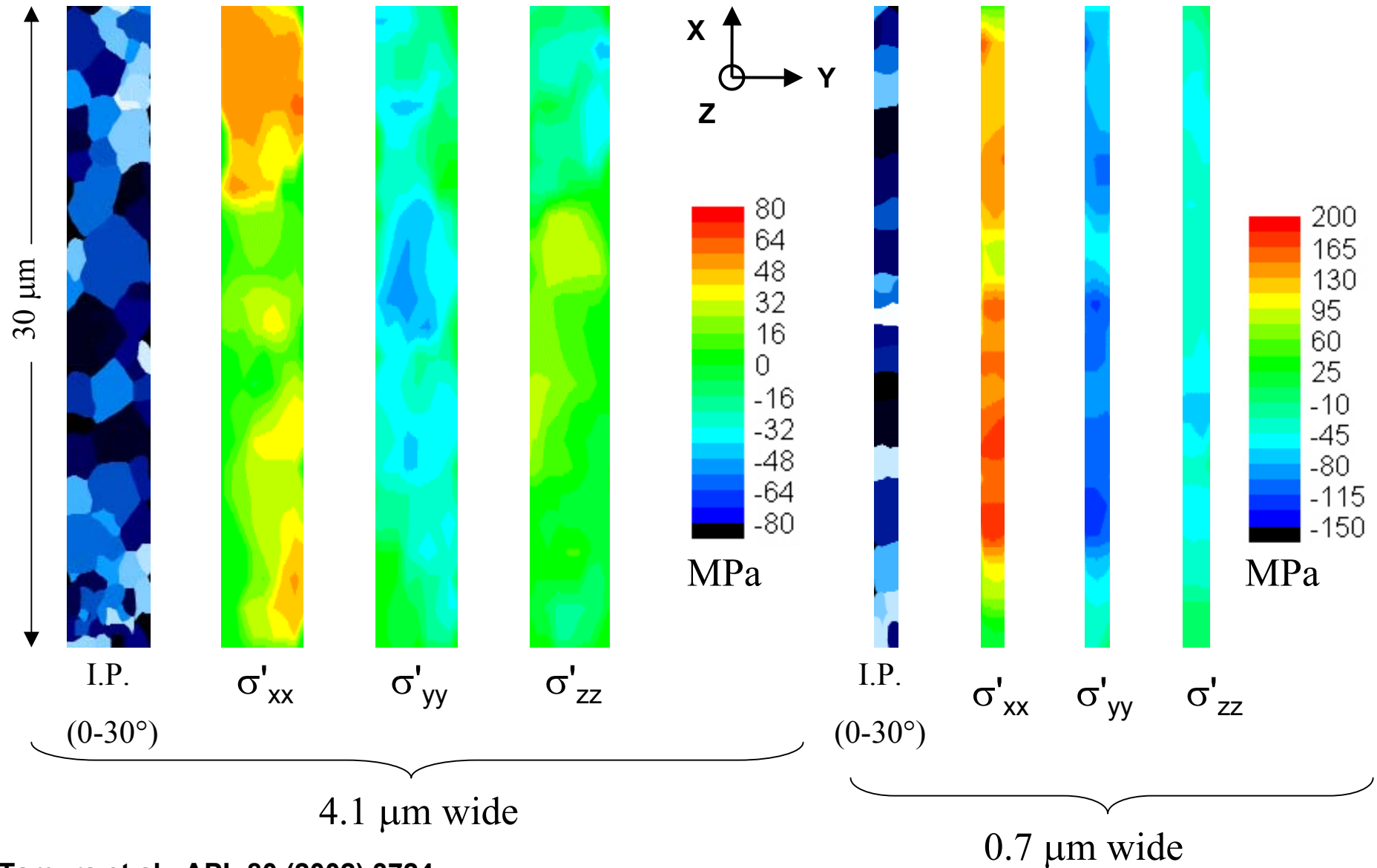
Photon energy range: 5-14 keV  
(monochromatic or white beam)



# Micro X-ray Diffraction at the ALS: BL 7.3.3

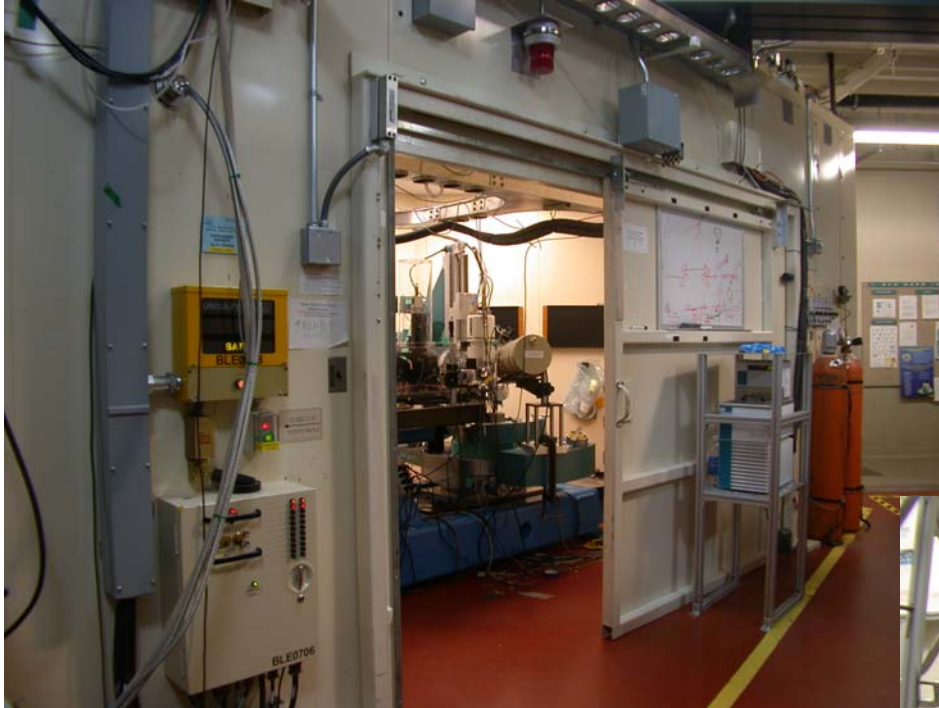


# Deviatoric stresses in passivated Al(Cu) lines





## Reuse of ALS Beamline 7.3.3



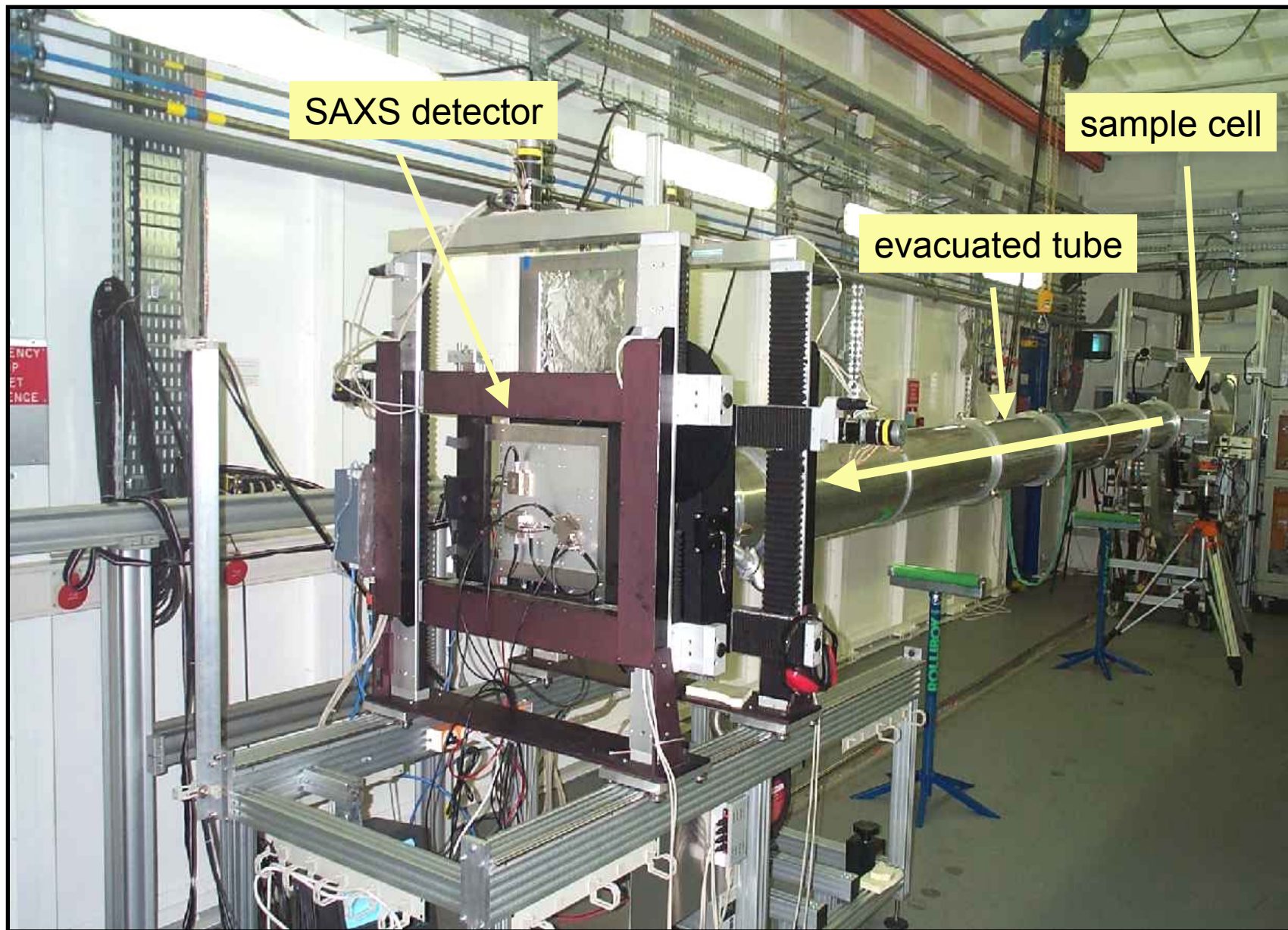
micro-diffraction program moving  
to a superbend beamline end 05

frees up BL 7.3.3 for SAXS

- detectors from BCSB
- equipment funds for sample stage  
+ flight tube etc.
- BL and detectors
  - a \$2M existing investment



# SAXS at the DUBBLE beamline: ESRF



# Measurement of Molecular Shape Using X-ray Scattering

## SAXS-WAXS on 7.3.3: Project schedule

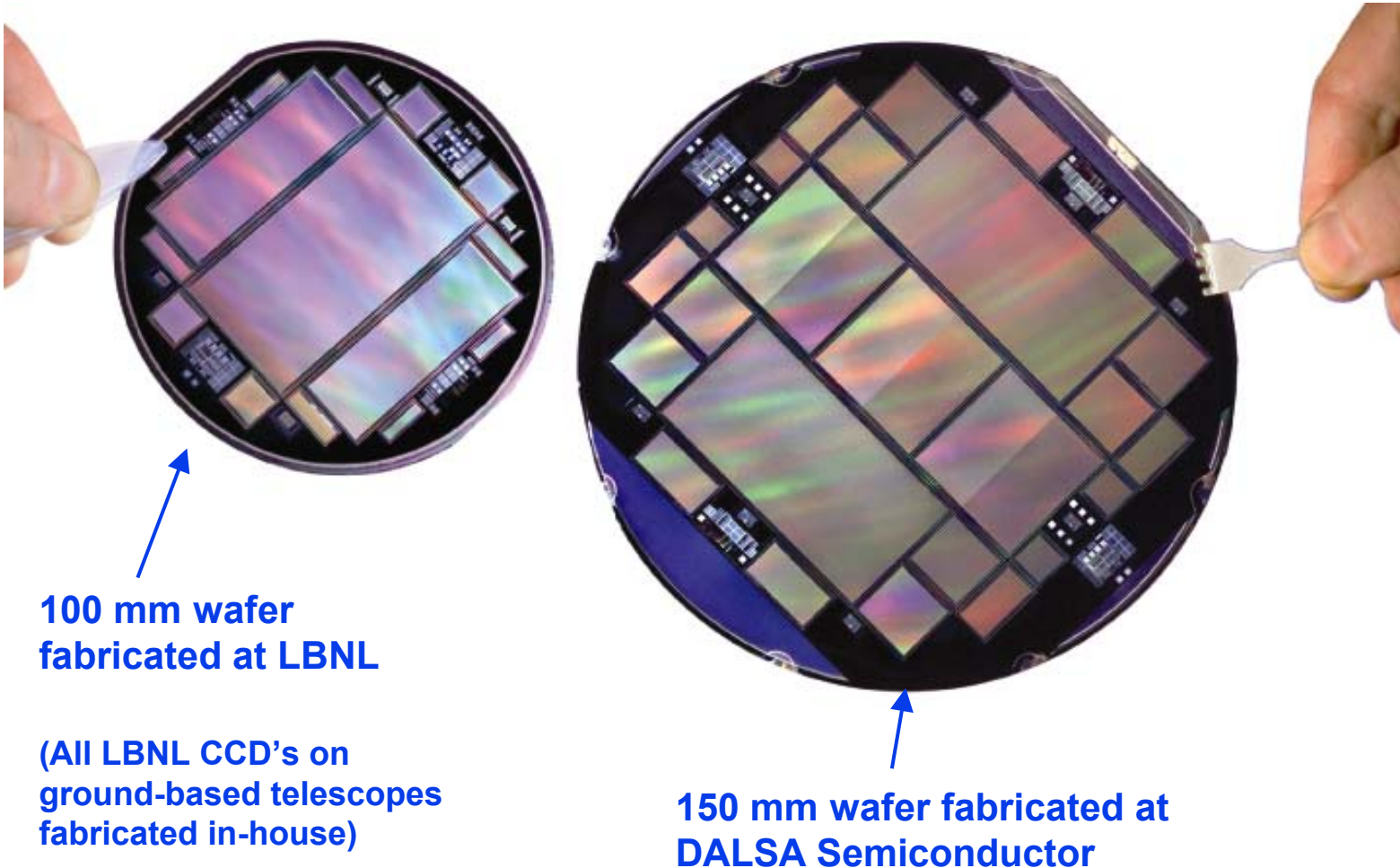
- beamline available late spring 06
- static SAXS – WAXS ~ fall 06

## Detectors

- initially using 2 ADSC Q4R detectors (readout 5 secs) from ALS protein crystallography program
- dynamics
  - developing fast CCDs (Denes , Padmore et al)
    - 200 fps, 16 bit (optical and direct x-ray)
  - starting collaboration on Si strip detectors for WAXS using existing ASICS



# LBNL fully depleted back illuminated CCDs: up to 650 microns thick

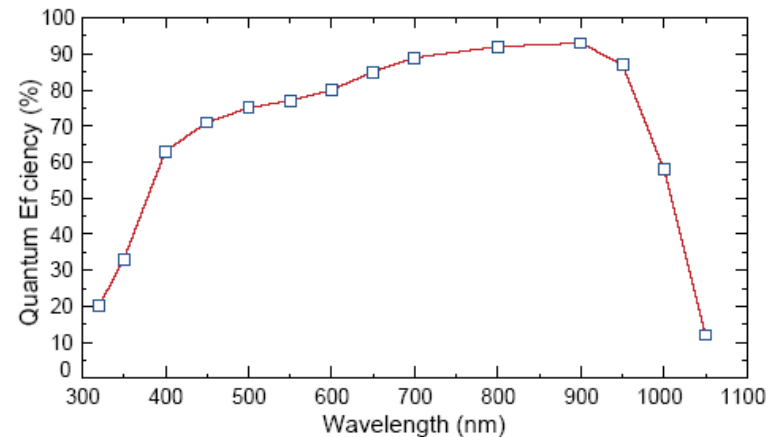
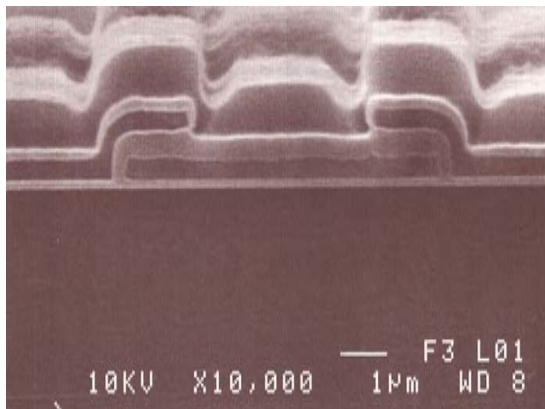
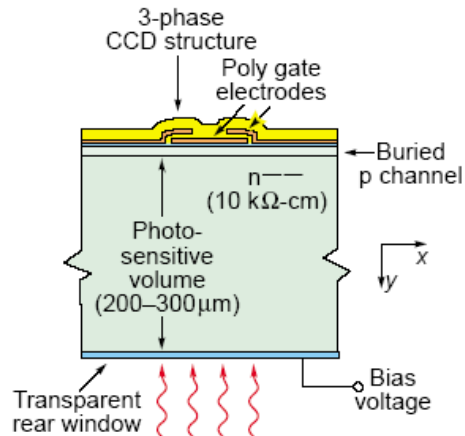


## Development of Fully Depleted, Back-Illuminated Charge Coupled Devices

C.J. Bebek, D.E. Groom, S.E. Holland, A. Karcher,  
W.F. Kolbe, N.P. Palaio, N.A. Roe, B.T. Turko, and G. Wang

Optical and Infrared Detectors for Astronomy, edited by James D. Garnett,  
James W. Beletic, Proc. of SPIE Vol. 5499 (SPIE, Bellingham, WA, 2004)  
0277-786X/04/\$15 · doi: 10.1117/12.552295

# LBNL fully depleted back illuminated CCDs



**Quantum efficiency of a 280 micron thick LBNL CCD with 15 micron pixels**

- depth gives optimized red quantum efficiency
- control of substrate bias gives optimized resolution

## Fully depleted back-illuminated p-channel CCD development

C.J. Bebek, J.H. Bercovitz, D.E. Groom, S.E. Holland, R.W. Kadel, A. Karcher, W.F. Kolbe, H.M. Oluseyi, N.P. Palaio, V. Prasad, B.T. Turko, and G. Wang

Lawrence Berkeley National Laboratory, 1 Cyclotron Road, Berkeley, CA

# Seeing through dust in the IR



LBNL CCD

Blue: H- $\alpha$  at 656 nm

Green: SIII at 955 nm

Red: 1.02  $\mu\text{m}$



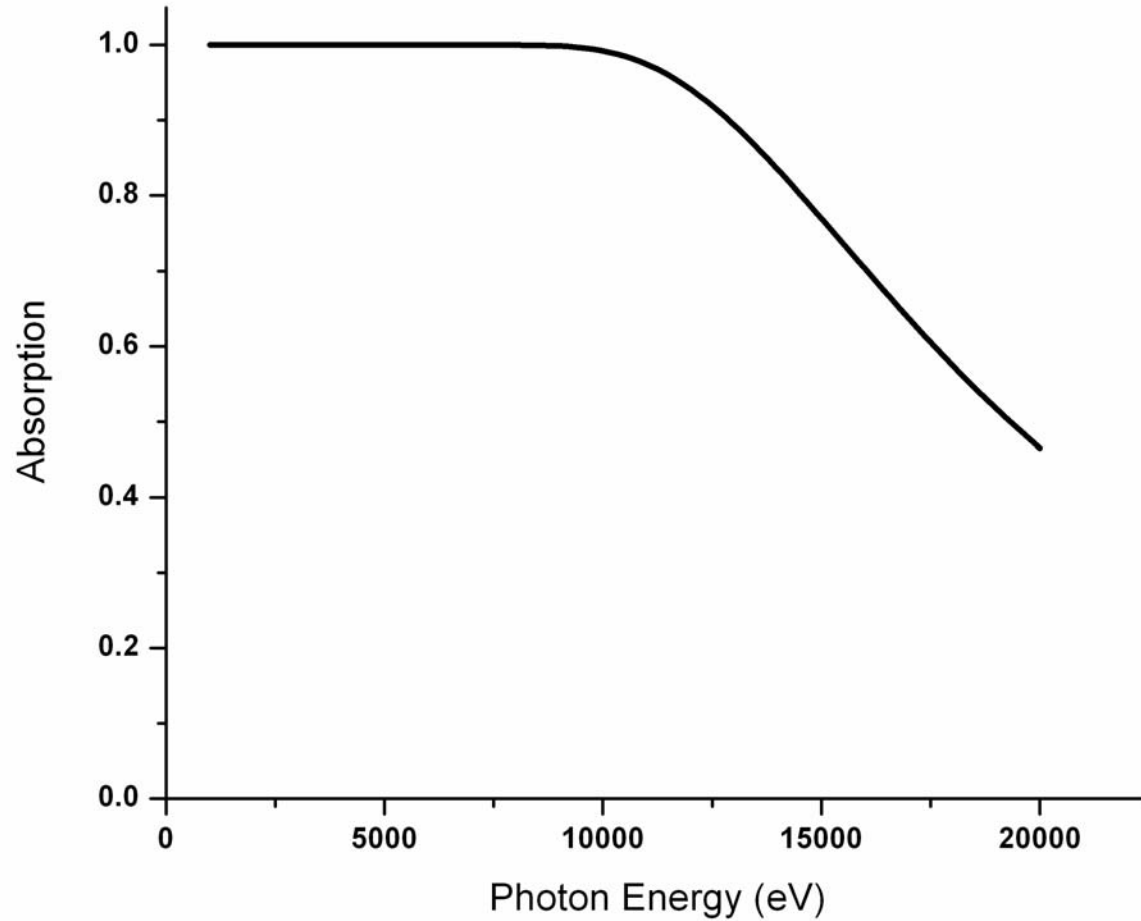
Planetary Nebula NGC 6853 (M 27) - VLT UT1+FORs1

ESO PR Photo 38a/98 ( 7 October 1998 )

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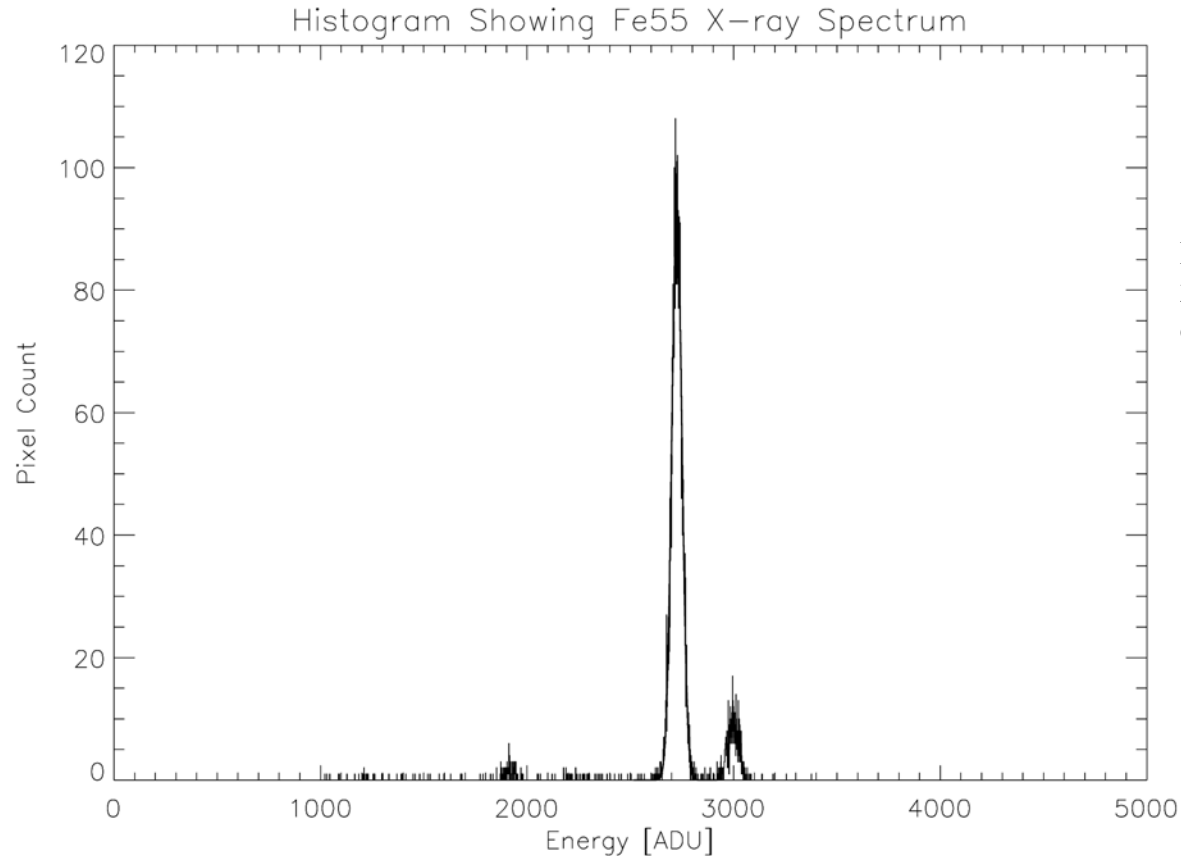


# Absorption: 650 micron thick CCD





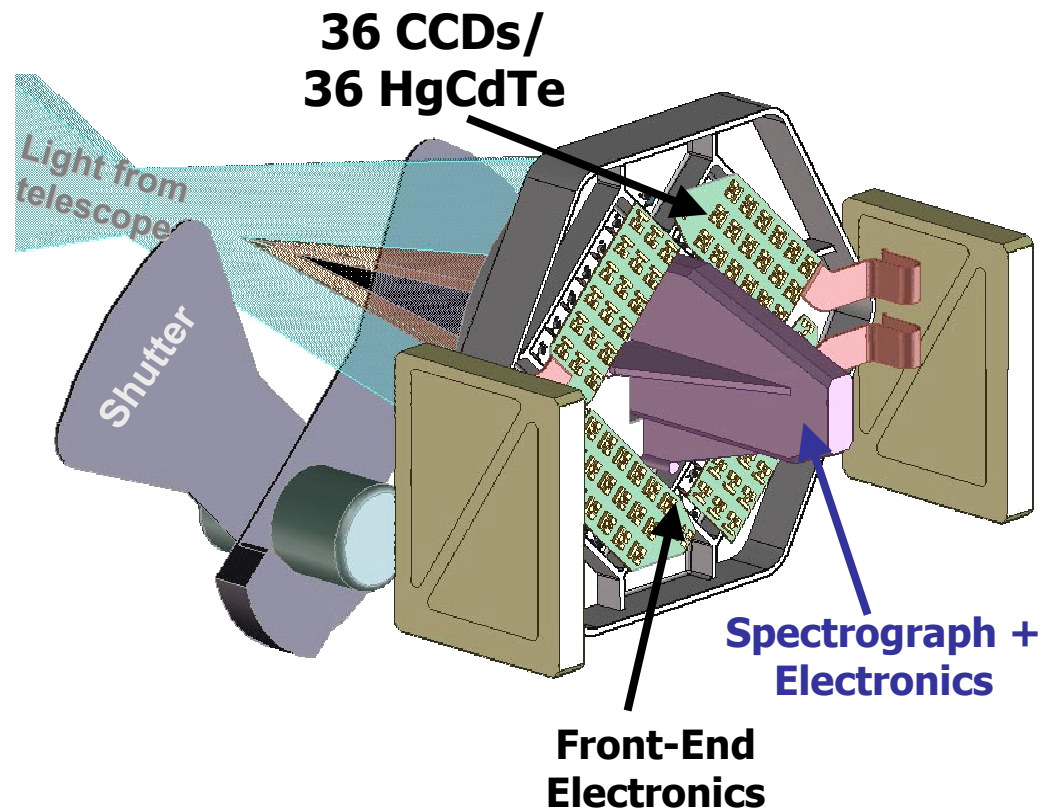
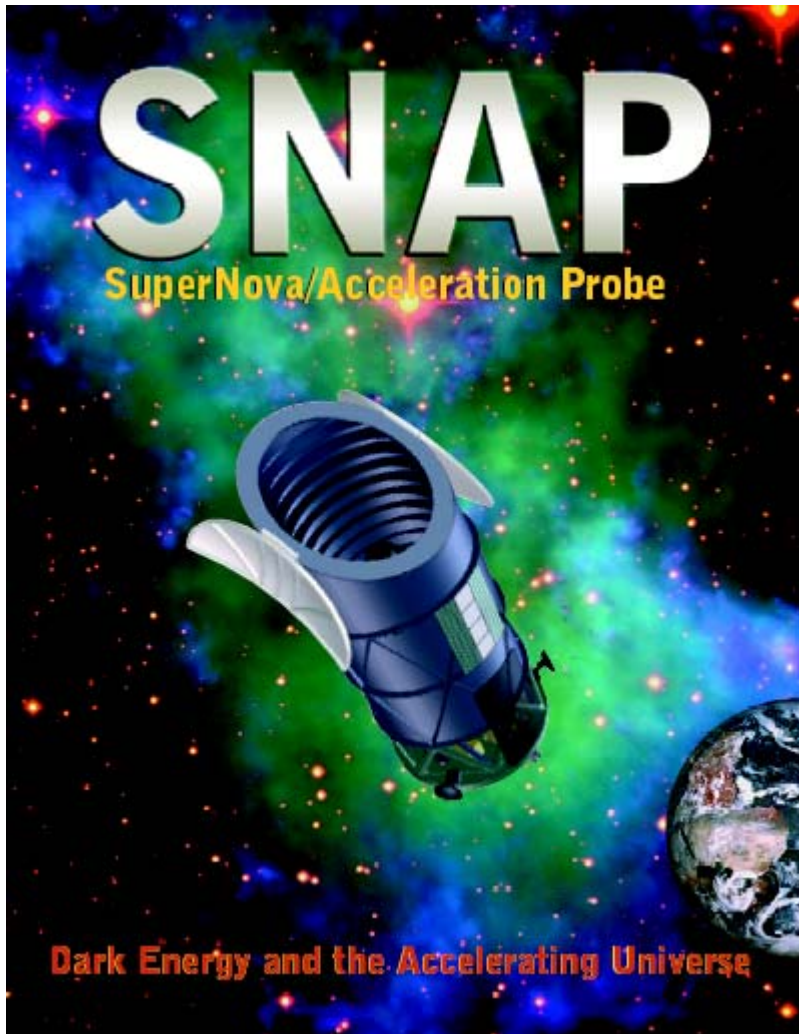
# Energy resolution: 650 micron thick CCD



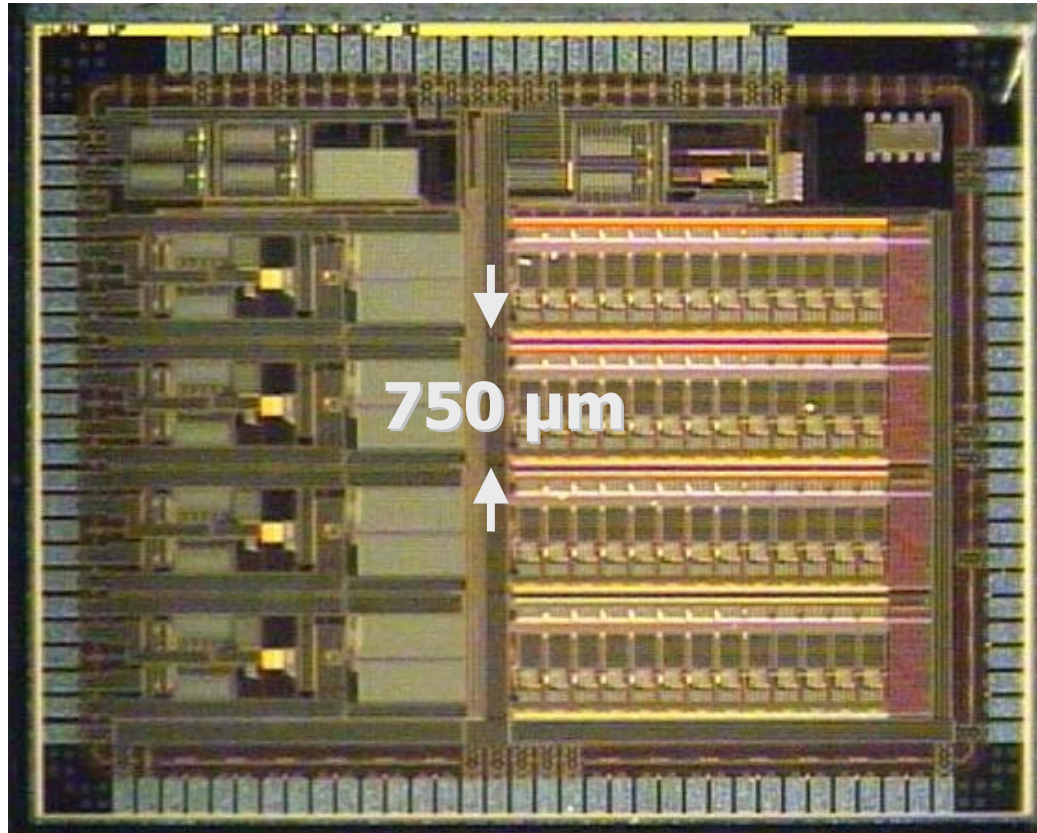
**Energy resolution:**  
 $24.7 \text{ ADU} * 3.65 \text{ eV/e-} * 2.35/1.68 \text{ ADU/e-}$   
or 126 eV

**X-ray histogram showing well resolved <sup>55</sup>Fe K $\alpha$  and K $\beta$  peaks and escape peak at ~2900 adu. The x-ray width,  $s = 24.7$  adu confirming good charge transfer and low noise. Read noise was 4.0 e- rms. Computed gain for the transistor used was 1.68 adu/e-.**

# Thick, deeply depleted, back illuminated CCDs and CMOS CCD readout used in SNAP

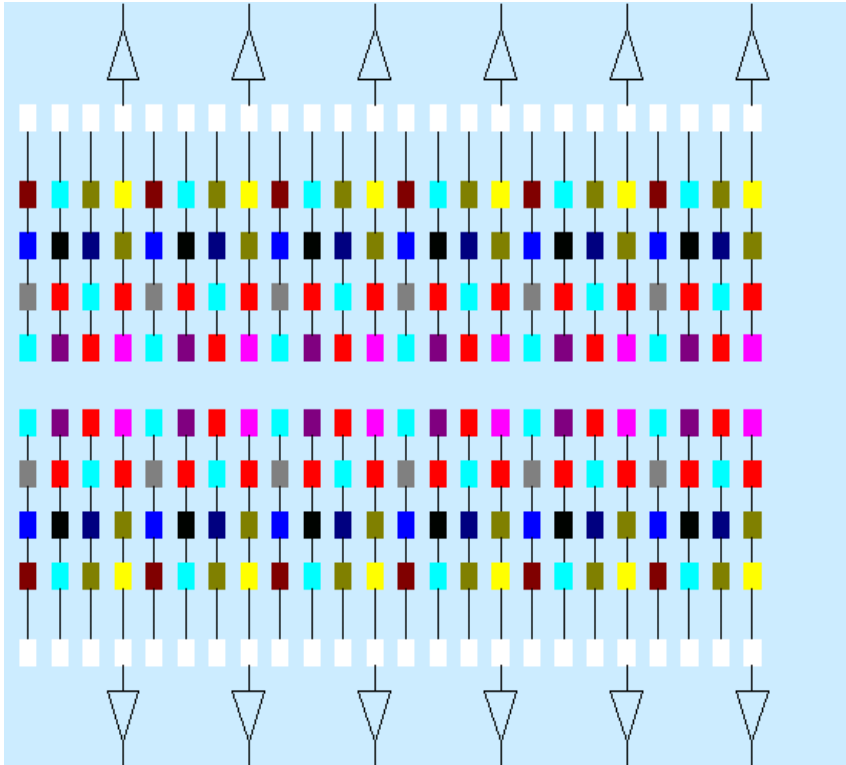


# SNAP CCD Readout Chip (CRIC)



- 16-bit multi-slope front-end
  - $2 e^-$  noise at 100 kHz
- 13-bit pipelined ADC
  - $INL < \pm 1.5 \text{ LSB}$
  - $DNL < \pm 0.5 \text{ LSB}$
- 10 mW/channel
- Space qualified
- 4 channels/chip for SNAP

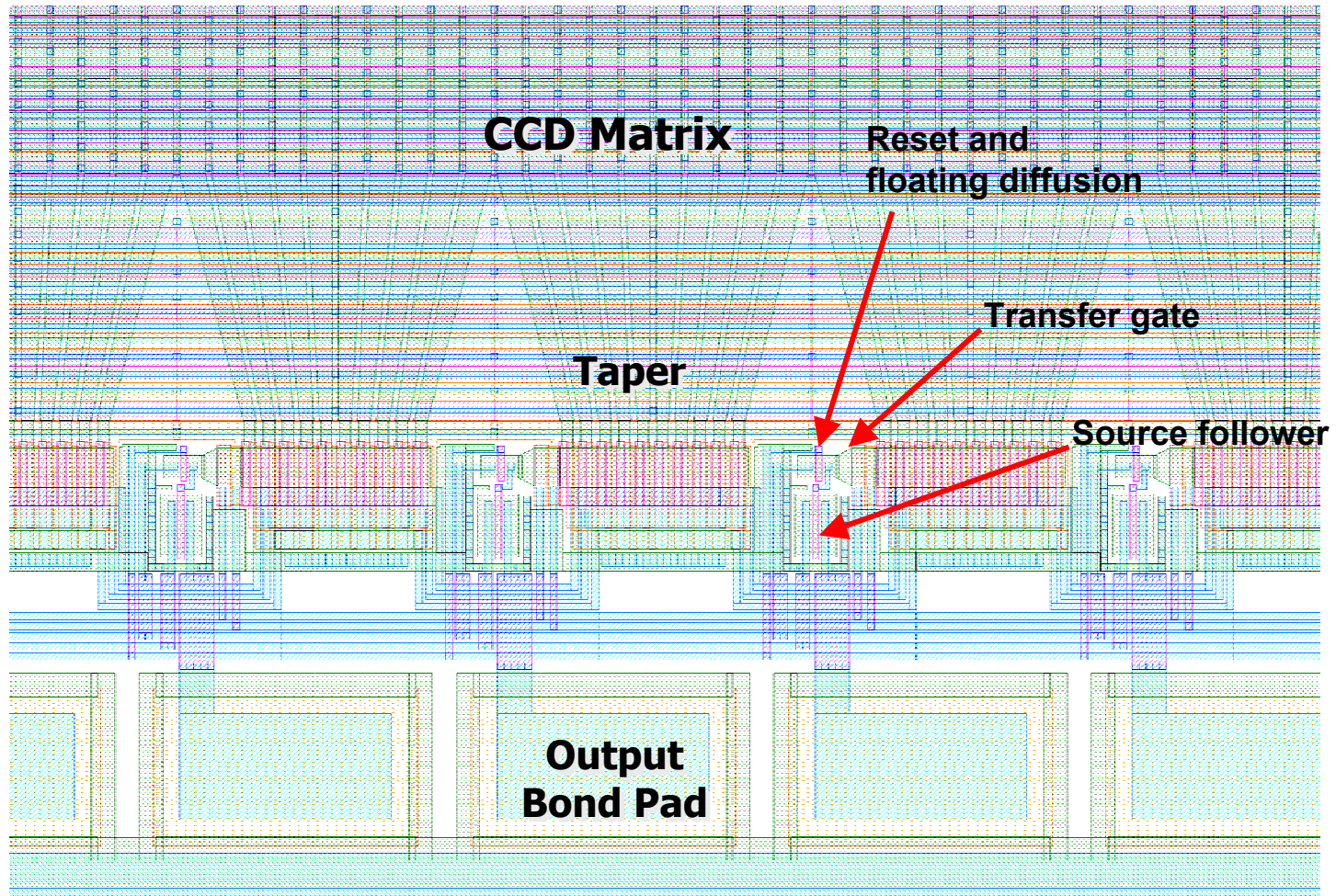
# Column Parallel CCDs



- Speed increased by  $N_{\text{PORTS}}$
- $N_H$  *large* enough to minimize the number of ADCs needed
- $N_H$  *small* enough to ensure readout speed required
- Only possible with high integration  
→ CMOS Integrated Circuits



# Prototype (almost) Column Parallel CCD Readout Structure



- 512 x 512, 30 micron pixels, 10 columns to 1 readout, double sided readout
- 512 KHz clock = 200 fps, < 10 e noise

# CP-CCDs for scattering

## Indirect

- phosphor – fiber – CP-CCD
  - suitable for hard x-ray SAXS-WAXS; easily covers large areas with a taper fiber optic
  - complex geometries (backscattering with hole in center of detector)

## Direct

- optical; dynamic light bio-microscopy
- x-ray
  - spectroscopy
  - hard and soft x-ray sensitivity (single photon, DQE=1)
  - very good pixel limited psf
  - array detector possible for backscattering
  - more challenging to cover large areas (max present size is 60 mm, 4K)

PIs and collaborators (Denes, Padmore, Holland, Bebek, Church....)